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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/519,330	04/25/2005	Peter Carmeliet	50304/056001	3636

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EXAMINER	
DEBERRY, REGINA M	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 02/06/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/519,330	CARMELIET ET AL.	
	Examiner	Art Unit	
	Regina M. DeBerry	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 November 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 9-13* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 9-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *3/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Status of Application, Amendments and/or Claims

The amendment filed 23 December 2004 has been entered in full. Claims 2-8 and 14 are cancelled.

Applicant's species election of antibodies binding on placental growth factor with traverse in the reply filed on 23 July 2004 is acknowledged. The traversal is on the ground(s) that examination of all antagonists recited in claim 10 would not present an undue burden on the Office. Applicant argues that each of the antagonists recited in claim 10 shares the common function that forms the general inventive concept (antagonists of placental growth factor). Applicant cites PCT Rule 13.1 and PCT Rule 13.2.

Applicant's arguments have been fully considered but are not found persuasive. Markush Practice for PCT (MPEP 1800) states that the requirement of a technical interrelationship and the same or corresponding special technical features as defined in PCT Rule 13.2, shall be considered to be met when the alternatives are of a similar nature. All alternatives have a common property or activity AND a common structure is present, i.e., a significant structural element is shared by all of the alternatives OR in cases where the common structure cannot be the unifying criteria, all alternatives belong to a recognized class of chemical compounds in the art to which the invention pertains. The antagonists recited in claim 10 lack a common structure and do not belong to a recognized class of compounds. Furthermore, the MPEP states when dealing with alternatives, if it can be shown that at least one Markush alternative is not

novel over the prior art, the question of unity of invention should be reconsidered by the Examiner (see art rejection below). The requirement is still deemed proper and is therefore made FINAL.

However, the Examiner will examine the species of antibodies binding on placental growth factor and small molecules binding on placental growth factor or VEGFR-1. The instant claims will be examined with respect to the those species. The other species remain withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected species, there being no allowable generic or linking claim. Applicant timely traversed the restriction (species election) requirement in the reply filed on 23 December 2004.

Claims 1, 9-13 are under examination.

Sequence Rules

The specification is not in compliance with 37 CFR 1.821-1.825 of the Sequence Rules and Regulations. When the description of a patent application discusses a sequence listing that is set forth in the "Sequence Listing" in accordance with paragraph (c) of the Sequence Rules and Regulations, reference must be made to the sequence by use of the assigned identifier (SEQ ID NO:), in the text and claims of the patent application. 37 CFR 1.821(a) presents a definition for nucleotide and/or amino acid sequences. This definition sets forth limits in terms of numbers of amino acids and/or numbers of nucleotides, at or above which compliance with the sequence rules is required. Nucleotide and/or amino acid sequences as used in 37 CFR 1.821 through

1.825 are interpreted to mean an unbranched sequence of four or more amino acids or an unbranched sequence of ten or more nucleotides. Please see MPEP section 2422.01.

The specification refers to sequences (page 5, line 29), but does not identify the sequences by their sequence identifiers. Sequences appearing in drawings should be referenced in the corresponding Brief Description thereof. See 37 C.F.R. §1.58(a) and §1.83.

Appropriate correction is required. Applicant must submit a response to this Office Action and compliance with the sequence rules within the statutory period set for response to this Office Action.

Information Disclosure Statement

The information disclosure statement(s)(IDS) filed (03 March 2005 and 17 March 2005) were received and comply with the provisions of 37 CFR §§1.97 and 1.98. They have been placed in the application file and the information referred to therein has been considered as to the merits.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1 and 10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which

applicant regards as the invention. The instant claims are indefinite because of the misspelling of "**placenta** growth factor". The instant specification teaches the spelling as "**placental** growth factor". Appropriate correction is required.

Claim Objections

Claims 11 and 12 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claims 11 and 12 depend from a claim, which is drawn to a method for treating a bone resorption disorder. The instant specification only teaches osteoporosis as a bone resorption disorder. Thus claims 11 and 12 fail to further limit the subject matter of the previous claim.

Claims 11 and 12 are objected to because the instant claims appear to read on the same scope. Claim 11 depends from claim 1. Claim 12 depends from claim 9, however, a method of treating a bone resorption disorder would require suppressing bone resorption (see claim 9). Thus the instant claims comprise very similar steps, which raises the question of similar scope. If the claims are not of similar scope, Applicant is asked to specifically point in the specification, the patentable distinction between the claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 9-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Niida *et al.* (reference submitted by Applicant, Journal of Experimental Medicine Vol. 190/2:293-298, 1999). The instant claims are drawn to a method for treating an individual diagnosed to have a disorder of bone resorption, said method comprising administering an antagonist of placental growth factor to the individual in an amount effective to treat said bone resorption disorder.

Niida *et al.* teach that vascular endothelial growth factor receptor (VEGFR-1) mediates chemotactic response of the cells to VEGF or placental growth factor 1 (PIGF-1)(page 294, lines 1-7). Niida *et al.* teach that mice with osteopetrosis (op/op mice; phenotype is abnormally dense bone) have a severe deficiency of osteoclasts caused by a deficiency in M-CSF (page 293, 1st paragraph). Niida *et al.* teach that VEGF can fully compensate for M-CSF in op/op mice in osteoclastic bone resorption. Niida *et al.* teach that VEGF is responsible for the end of osteopetrosis in op/op mice (page 294, lines 1-15). Niida *et al.* teach the administration of VEGF and PIGF-1 in osteopetrosis mice. VEGF and PIGF-1 were able to recruit osteoclast (page 294, Results and Discussion, 1st paragraph and Table 1). Niida *et al.* teach that injection of anti-VEGFR-1 antibody decreased osteoclast (page 295, lines 1-16 and Table II). Niida

et al. teach that VEGF can support the bone-resorbing function of osteoclasts (page 295, 1st paragraph).

Niida *et al.* do not actually administer anti-VEGFR-1 antibodies (small molecule binding on VEGFR-1) to an individual diagnosed with a disorder of bone resorption (osteoporosis). Niida *et al.* administer anti-VEGFR-1 antibodies to mice diagnosed with osteopetrosis. However, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the method of Niida *et al.* by administering antibodies against VEGF, VEGFR-1 or PIGF with a reasonable expectation of success. The motivation and expected success is provided by Niida *et al.* who teach that mice with osteopetrosis have a severe deficiency of osteoclasts caused by a deficiency in M-CSF (and VEGF can fully compensate for M-CSF) in op/op mice. VEGF causes osteoclastic bone resorption, thus antibodies made against VEGF, VEGFR-1 or PIGF-1 would decrease bone resorption.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Regina M. DeBerry whose telephone number is (571) 272-0882. The examiner can normally be reached on 9:00 a.m.-6:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda G. Brumback can be reached on (571) 272-0961. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

RMD
1/28/06

MARIANNE P. ALLEN
PRIMARY EXAMINER
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2/2/06